

REMARKS

Claims 18, 20-23, 29, 31-34, 65, and 66 are pending in the application.

Claims 23, 32, and 33 stand “withdrawn from further consideration as being drawn to a nonelected species” (Office Action, page 2). Upon allowance of generic claim 18, Applicants respectfully request rejoinder and examination of claims 23, 32, and 33, which depend from, and are therefore fully embraced by, generic claim 18 (see, e.g., MPEP § 809.02(c)).

Applicants have amended claims 18 and 65 as follows. Applicants have inserted “unsubstituted” immediately before the recitation of “alkyl or alkenyl” in the definition of subvariable “X” to clarify that X is an unsubstituted alkyl or alkenyl moiety. Applicants have deleted “O-sulfonic acid” from the listing of permissible substituents for subvariable “Z” when Z is Z is alkyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl. Support for these amendments can be found throughout the Specification, e.g., at page 5, lines 13-17, page 8, line 1, page 10, lines 1-5, page 11, lines 28-30; and claims 30, 33, and 34 as originally filed.

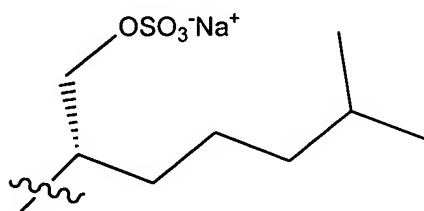
Claim 29 has been amended to comport in scope with claim 18 as currently amended.

No new matter is introduced by these amendments.

Rejections under 35 U.S.C. 102(b)

Claims 18, 21, 22, 29, 31, and 65 are rejected as being anticipated by Riccio et al., *Tetrahedron* **1985** 41, 6041-6046 (Riccio). The Office relies upon the disclosure of compounds 1 and 4 in Riccio.

Compounds 1 and 4 in Riccio are steroid compounds in which the substituent corresponding to R¹⁷ in the formula delineated in claim 18 has the following structure:



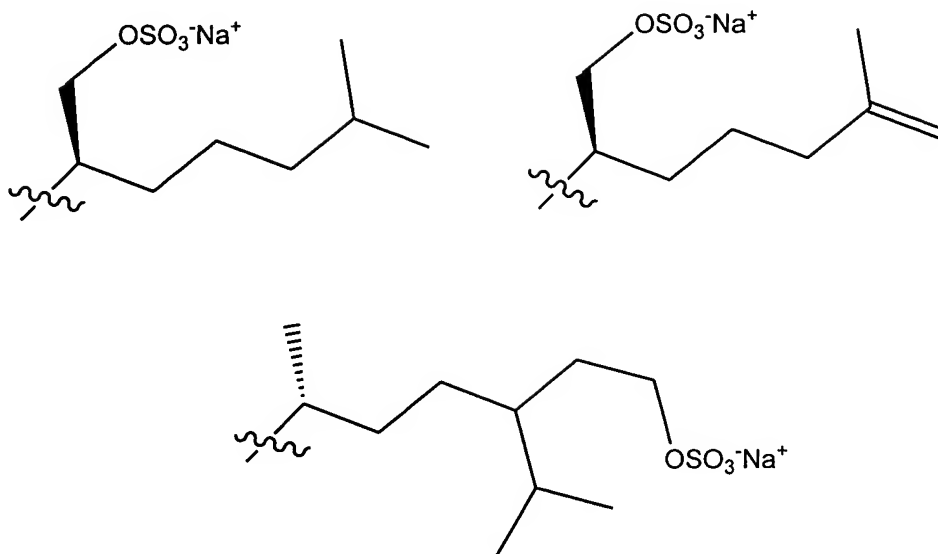
R¹⁷ in claims 18 and 65 is further defined as having the general formula “-X-Y-Z.” Accordingly, the substituent corresponding to R¹⁷ in Riccio compounds 1 and 4 is one in which X is alkyl, Y is a bond, and Z is an alkyl moiety that is substituted with -OSO₃ Na⁺ (i.e., an O-sulfonic acid sodium salt).

However, claims 18 and 65 as currently amended exclude O-sulfonic acid as a permissible substituent for Z when Z is an alkyl moiety. As such, compounds 1 and 4 disclosed in Riccio fall outside of the scope of claims 18 and 65 as currently amended.

Applicants submit that Riccio does not anticipate independent claims 18 and 65 as currently amended because Riccio does not teach every element of claims 18 and 65 as currently amended. Since claims 21, 22, 29, and 31 depend from claim 18, they also are not anticipated by Riccio. Applicants respectfully request withdrawal of the rejection and that the rejection not be applied to claims 23, 32, and 33.

Claims 18, 21, 22, 29, 31, and 65 are rejected as being anticipated by McKee et al., *J. Med. Chem.* **1994** 37, 793-797 (McKee). The Office relies upon the disclosure of compounds 13, 15-18, and 21 in McKee.

Compounds 13, 15-18, and 21 in McKee are steroid compounds in which the substituent corresponding to R¹⁷ in the formula delineated in claim 18 has one of the following structures:



More specifically, each of the above substituents corresponding to R^{17} in the McKee compounds are ones in which X is alkyl or alkenyl, Y is a bond, and Z is an alkyl moiety that is substituted with $\text{-OSO}_3^-\text{Na}^+$ (i.e., an O-sulfonic acid sodium salt).

Applicants submit that the McKee compounds also fall outside of the scope of claims 18 and 65 as currently amended for the reasons provided above concerning Riccio.

Applicants respectfully request reconsideration and withdrawal of the rejection in view of the foregoing remarks and amendments to claim 18, 29, and 65.

Rejections under 35 U.S.C. 103(a)

Claim 20 is rejected as being unpatentable over McKee. According to the Office Action:

The instant claim differ from the reference by reciting a isomer, i.e., 3 α , 6 α - isomer, of stigmastane-- 3 β , 5 α , 6 β , 8 β , 15 α , 16 β , 29-hepto, 29-sulfate. However, a compound that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. *In re Norris*, 179 F.2d970, 84 USPQ 458 (CCPA 1970) (Office Action, page 4).

Applicants respectfully disagree and request reconsideration and withdrawal of the rejection for any of the following independent reasons.

First, the Examiner has extracted the fact specific holdings from *In re Norris* (cited in the above-quoted passage from the Office Action) and applied them as a *per se* rule for analyzing the obviousness of chemical structures. This is improper as it is well established that the Examiner cannot rely on “per se” rules of obviousness. Second, the prior art must provide the skilled artisan with the motivation to modify one or more reference compounds to arrive at the claimed compounds. The reference compound relied upon by the Office in the present rejection is an “inactive” compound and therefore lacking in any apparent practical utility. When reference compound(s) lack utility, as is the case here, then such motivation does not exist, and the *prima facie* case is not established. These points are discussed in more detail below.

I.

Applicants point out that there are no *per se* rules of obviousness of any kind, let alone *per se* rules concerning the obviousness of a claimed compound versus a prior art isomer. This assertion is not merely argumentation, but a fact of law:

We once again hold today that our precedents do not establish any *per se* rules of obviousness, just as those precedents themselves expressly declined to create such rules. Any conflicts as may be perceived to exist derive from an impermissible effort to extract *per se* rules from decisions that disavow precisely such extraction *In re Ochiai* 37 USPQ2d 1127, 1133 (Fed. Cir. 1995) (underline emphasis added; italics in original).

The obviousness inquiry under 35 U.S.C. § 103(a) is “highly fact-specific by design.” *Ochiai* at 1131. “Whether invention exists over prior art isomers and homologues is a question to be decided in each case.” *In re Henze* 85 USPQ 261, 264 (CCPA 1950). The Examiner has cited a case (*In re Norris*) where a claimed compound or genus was held as being obvious over a prior art isomer. This cited case, however, does **not** in and of itself establish or imply that there exists any general obviousness rule that a compound claim is obvious if the prior art discloses an isomer thereof. As the Federal Circuit explained in *Ochiai*:

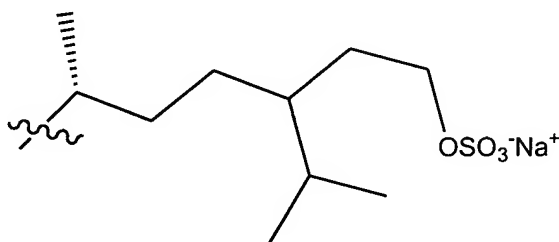
...the examiner incorrectly drew from *Durden*, a case turning on specific facts, a general obviousness rule: namely, that a process claim is obvious if the prior art references disclose the same general process using similar starting materials.⁵ No such *per se* rule exists. Mere citation of *Durden*, *Albertson*, or any other case as a basis for rejecting process claims that differ from the prior art by their use of different starting materials is improper, as it sidesteps the fact-intensive inquiry mandated by section 103. In other words, there are not ‘*Durden* obviousness rejections’ or ‘*Albertson* obviousness rejections,’ but rather only section 103 obviousness rejections. *Ochiai* at 1131 (italics in original).

The views expressed in *Ochiai* affirm that there are no *per se* rules of obviousness-- even where the structural difference between the claimed and prior art compounds is relatively small, such as when the claimed and prior art compounds are related as isomers.

II.

McKee discloses the isolation of various sulfated sterols and their cytoprotective effects against HIV-1 and HIV-2.

The Office relies upon the disclosure of the sulfated sterol “stigmastane-- 3 β , 5 α , 6 β , 8 β , 15 α , 16 β , 29-hepto, 29-sulfate” (Office Action, page 4) in the present rejection. It is Applicants understanding that “stigmastane-- 3 β , 5 α , 6 β , 8 β , 15 α , 16 β , 29-hepto, 29-sulfate” refers to compound 13 in McKee. Compound 13 is a sulfated sterol in which the substituent corresponding to R¹⁷ in the formula delineated in claim 18 has the following structure:



(i.e., an alkyl moiety that is substituted with -OSO₃Na⁺ (i.e., an O-sulfonic acid sodium salt). As discussed elsewhere, compound 13 in McKee falls outside of the scope of the present claims.

McKee also discloses that compound 13 was “inactive” against HIV “at the highest tested concentrations (100 mg/mL)” (McKee, pages 795, left column, emphasis added). Moreover, compound 13 of McKee was observed to provide “no protection of cells to HIV-induced killing” (McKee, pages 793, Table 1, emphasis added). These observations are indicative that compound 13 is a biologically inactive compound with no apparent utility as a therapeutic agent.

In order for a *prima facie* case of obviousness of a chemical composition to be established there must be “structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions.” *In re Dillon* 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (*In Banc*). The Federal Circuit in *Dillon* also held that the *prima facie* case can be rebutted with a showing “that the prior art is so deficient that there is no motivation to make what might

otherwise appear to be obvious changes,” citing, for example, *In re Stemniski*, 444 F.2d. 581, 170 USPQ 343 (CCPA 1971). *In re Dillon* 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (*In Banc*).

Stemniski established that a presumption of unpatentability is not created when the structurally similar reference compounds lack utility because there is no motivation to prepare related compounds:

“[w]here the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one of ordinary skill in the art an isomer, homologue, or analog or related structure, when that mythical, but intensely practical, person knows of no ‘practical’ reason to make the reference compounds, much less any structurally related compounds *Stemniski* at page 347.

The Federal Circuit in *Dillon* distinguished *Stemniski*, stating:

Thus, *Stemniski*, rather than destroying the established practice of rejecting closely-related compounds as *prima facie* obvious, qualified it by holding that a presumption is not created when the reference compound is so lacking in any utility that there is no motivation to make close relatives *In re Dillon* 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (*In Banc*).

The Office has argued that the motivation to prepare the claimed compounds stems from the fact that “[t]he instant claim differ from the reference by reciting a isomer, i.e., 3 α , 6 α - isomer, of stigmastane-- 3 β , 5 α , 6 β , 8 β , 15 α , 16 β , 29-hepto, 29-sulfate” (Office Action, page 4, emphasis added). As mentioned elsewhere, the compound relied upon by the Office falls outside of the scope of the present claims as currently amended. **As such, the present claims as currently amended do not recite such an isomer.**

In any event, the above case law clearly established that structural similarity alone is insufficient to create the *prima facie* case of obviousness. The prior art must also provide the skilled artisan with the motivation to modify one or more reference compounds to arrive at the claimed compounds. Compound 13 of McKee is a biologically inactive compound with no apparent utility as a therapeutic agent. When reference compound(s) lack utility, as is the case with the non-cytoprotective, HIV-inactive compound 13 of McKee, then such motivation does

not exist, and the *prima facie* case is not established. Thus, one of ordinary skill in the art would not be motivated to prepare the claimed compounds in view of the teachings of McKee.

In summary, Applicants submit the motivation or suggestion to prepare the claimed compounds is found only in Applicants' Specification. For the reasons set forth above, the Examiner has failed to establish that a person of ordinary skill in the art would have been motivated to make Applicants' claimed compounds in view of the teachings of McKee and therefore the *prima facie* case of obviousness is incomplete. Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that all claims are in condition for allowance.

Enclosed is a \$60 check for the One-Month Petition for Extension of Time fee. Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No.: 10634-002002.

Respectfully submitted,

Date:

November 18, 2005

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